REMARKS

Entry of the foregoing amendments, reconsideration and reexamination of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, and in light of the remarks which follow, are respectfully requested.

By the present amendments, the claims have been rewritten in an effort to obviate the outstanding § 112 issues. All of the newly submitted claims correspond to the elected invention and are directed to a nucleic acid sequences encoding a human T1R2 polypeptide, which comprises a taste receptor (GPCR) involved in sweet taste transduction or are directed to DNA constructs or vectors containing such a human T1R2 nucleic acid sequence.

Additionally, all of the nucleic acid sequence claims now require that the nucleic acid sequences encode an hT1R2 polypeptide that when expressed in association with a nucleic acid sequence encoding the human T1R3 polypeptide contained in SEQ ID NO: 4, results in a heteromeric sweet receptor that responds to sweet taste stimuli. Therefore, as a result of this amendment, the claims are limited to nucleic acid sequences that encode functional T1R2 receptor polypeptides. It is anticipated that these amendments should obviate all of the outstanding § 112 rejections. Support for the newly inserted limitation (that human T1R2 polypeptide associates with human T1R3 polypeptide to produce a human T1R2/T1R3 taste receptor) may be found *e.g.*, in examples 8 and 9. These examples relate to experiments conducted using hT1R2/hT1R3 expressing cells

showing that this heteromeric receptor specifically responds to both natural and artificial (synthetic) sweet stimuli.

Turning now to the Office Action, Applicants confirm their previous election of a nucleic acid sequence encoding a human hT1R2 polypeptide. This Restriction Requirement has been maintained. As noted above, all of the newly submitted claims correspond to the elected Group.

The objections to the Specification are noted.

The objections to the hyperlink are obviated by amendments amending the appropriate paragraphs pages 16 and 39 to delete references to hyperlink.

The Specification at page 10 has also been amended to include the Serial Number for the application referred to by attorney docket number.

Claims 1-5, 10-11, 14-15, 24-25, 24-25, 44-45, 56-58, 68-69, 80-81, 90-119, 201-202, and 213-214 were rejected under 35 U.S.C. § 112 second paragraph. The basis of these rejections are not specifically addressed herein as the rejections are moot in view of the present amendments. The new claims do not contain the language or noted criticisms of the prior claims.

Claims 1, 4-11, 14-41, 44-51, 59-119, 201-208 and 211-222 were rejected under 35 U.S.C. § 112 first paragraph as allegedly being broader than the enabling disclosure. This rejection is respectfully traversed to the extent it may be applicable to the claims as amended.

Essentially, the Examiner takes the position that the Specification only provides sufficient enabling support for the exemplified human T1R2 nucleic acid sequence contained in SEQ ID NO: 20 which encodes a polypeptide human taste receptor that responds to sweet taste stimuli when expressed in association with hT1R3 receptor polypeptides. (The Office Action only mentions sucrose which is correct, however, the Specification examples further exemplify that the T1R2/T1R3 receptor responds to other sweet stimuli, *e.g.*, the artificial sweeteners monellin and aspartame, and that the dose responses with specific sweet compounds correlate to human sweet taste detection thresholds.)

More specifically, the Examiner indicates that the Specification does not provide adequate enablement support as to how to make nucleic acid sequences which hybridize thereto and/or encode polypeptides which are not identical to the polypeptides contained in SEQ ID NO: 21 which retain the desired functionality (encode a functional sweet taste receptor polypeptide). This rejection is respectfully traversed.

As recognized by the Examiner the subject application clearly describes that the exemplified T1R2 nucleic acid sequence, when expressed in association with a human T1R3 polypeptide, yields a heteromeric taste (sweet) receptor that specifically responds to natural and artificial sweet ligands. (*See* examples 7-9 and 11 of the subject application which contain experimental data showing that receptors comprising hT1R2 polypeptides respond specifically in assays when

contacted with sweet compounds). Still further, the as-filed application describes assays, particularly numerous cell-based assays, that are useful in detecting the response of the subject T1R2/T1R3 taste receptor to ligands, *i.e.*, sweet taste stimuli.

Particularly, the Specification contains extensive description and exemplification of a variety of appropriate assays and expression systems that can be used to express a hT1R2 nucleic acid sequence in association with a hT1R3 nucleic acid sequence, and screen whether the particular hT1R2 nucleic acid sequence results in a functional sweet taste receptor based on whether it retains the capability of specifically responding to sweet taste stimuli. Based on this disclosure, one skilled in the art would be able, absent the exercise of undue experimentation, to express nucleic acid sequences that hybridize under stringent conditions to the exemplified hT1R2 nucleic acid sequence and/or which encode T1R2 polypeptides having at least 90% sequence identity to the disclosed hT1R2 polypeptide sequence, to express same in association with the disclosed hT1R3 nucleic acid sequence, and ascertain which nucleic acid sequences encode functional sweet taste receptors. This could be effected by a nucleic screening process and would not require a specific teaching, as to what hT1R2 residues are required for functionality to provide an enabling disclosure.

Contrary to the Office Action, it would be reasonably anticipated, *i.e.*, predictable that this screening process would reproducibly yield variant hT1R2

nucleic acid sequences that encode a functional sweet taste receptor (when expressed in association with disclosed hT1R3 nucleic acid sequence).

Applicants further note that with respect to the enablement rejection of record that the claims have been narrowed to require that the nucleic acid sequence hybridizes under defined high stringency conditions and/or encodes a polypeptide having at least 90% sequence identity with the exemplified hT1R2 polypeptide. Accordingly, based on the language and limitations of the pending claims it would be anticipated that the claims would only encompass nucleic acid sequences encoding polypeptides having a high degree of sequence identity with hT1R2 polypeptide. Therefore, as the claims embrace a much similar genus of nucleic acid sequences than previously, this would be anticipated to significantly reduce the amount of experimentation required to identify functional T1R2 variants meeting the limitations of the claims.

Applicants further respectfully traverse the rejection on the basis it is inconsistent with PTO practice and many granted patents directed to novel genes. Particularly, it is routine for the Patent Office when examining applications directed to gene sequences, that when an Applicant identifies a novel gene with a known function and further teaches a means for identifying functional variants of the gene, for the Patent Office to allow Applicants to claim a genus of variants of the gene; provided that the scope of the genus is reasonable (based on the teachings of the application). Applicants respectfully

submit that the claimed genus of hT1R2 sequence claimed herein is reasonable based on the as-filed disclosure and normal PTO practice, especially given the fact that a number of suitable assays are exemplified in the Specification which would allow one skilled in the art to identify variants of the exemplified hT1R2 nucleic acid sequence (contained in SEQ ID NO: 21) that encode functional sweet taste receptor polypeptides.

In further support of the enablement rejection, the Examiner cites to a Hoon et al., Cell, 96:541-551 (1999) article which is cited based on its disclosure of difficulties in determining "the ligand/taste specificity of T1R and T2R using a variety of strategies".

However, Applicants submit that the article is not germane since it does not take into account later information , contained in the present application, relating to operative heterologous expression systems that <u>have identified the ligand specificity of the subject hT1R2 receptor</u>, namely it specifically responds to sweet taste stimuli. Therefore, contrary to the rejection, the subject Specification provides more than "general guidance", rather it provides assays and expression systems that have been shown to be operative and establish that the subject nucleic acid sequence encodes a taste receptor that responds to both artificial and natural sweet compounds.

Based on the foregoing, withdrawal of the enablement rejection of claims 1, 4-11, 14-41, 56-119, 201-208 and 211-222 is therefore respectfully requested.

Claims 1, 4-5, 7-11, 14-15, 17-41, 44-45, 47-53, 56-57, 59-119, 201-202, 204-208, and 211-222 further stand rejected under 35 U.S.C. § 112 first paragraph based on written description grounds. Similar to the prior discussed § 112 enablement objection, the Examiner questions whether the Specification would place a skilled artisan in "possession" of the genus of hT1R2 variants embraced by the claims.

At the outset, Applicants again respectfully note that the scope of the claims have been revised as set forth in new claim 235 to only encompass hT1R2 nucleic acid sequences that hybridize under defined high stringency conditions to the exemplified hT1R2 nucleic acid sequence and/or which encode polypeptides having at least 90% sequence identity to the human T1R2 polypeptide contained in SEQ ID NO: 21 and to further require that the claimed hT1R2 nucleic acid sequences encode a functional sweet taste receptor (when expressed in association with the hT1R3 polypeptide contained in SEQ ID NO: 4).

Applicants respectfully submit that for the same reasons set forth in the traversal of the enablement rejection, the Specification provides sufficient teaching to place one skilled in the art in possession of functional hT1R2 variants as claimed. Particularly, the as-filed Specification describes and exemplifies cell-based assays and expression systems that demonstrate unequivocably that the subject hT1R2 receptor specifically responds to sweet taste stimuli. Therefore, these expression systems and assays place one skilled

in the art in possession of hT1R2 variants according to the claims, *i.e.*, variants that encode functional sweet taste receptors when expressed in association with a hT1R3 polypeptides.

Moreover, while Applicants concede that no functional hT1R2 variants are exemplified herein, it would be routine, based on the teachings in the application, to produce and identify functional variant hT1R2 nucleic acid sequences, *i.e.*, those which when expressed in association with hT1R3 specifically respond to sweet stimuli. This would be conducted by routine screening methods using screening methods disclosed in the subject patent application.

The Examiner further relies on a Eli Lilly case in support of the written description rejection. However, this reliance is respectfully submitted to be improper.

Unlike the Lilly case cited by the Examiner, the subject Specification provides information relating to both the sequence (structure) of the genomic hT1R2 nucleic acid sequence and corresponding hT1R2 polypeptide as well as identifying ligands that specifically bind and activate this receptor (function). Accordingly, Applicants disclose information in this application which defines the structure and function of the claimed nucleic acid sequences. Thus, unlike Lilly, the structure/function test is satisfied.

Therefore, the facts in Lilly case are not controlling with respect to the facts herein. Unlike in Lilly, the subject Specification provides substantial sequence disclosure (the complete sequence of the hT1R polypeptide and gene are provided) and the Specification further provides assays for identifying functional variants of this sequence thereby constructively placing a skilled artisan in possession of the claimed invention.

Based on the foregoing, withdrawal of the § 112 written description based on rejection of claims 1, 4-5, 7-11, 14-15, 17-41, 44-45, 47-53, 56-57, 59-119, 201-202, 204-208, and 211-222 is respectfully requested.

Claims 1, 6, 14-16, 22-26, 32-36, 44-45, 56-57, 66-70, 76-82, 88-94, 100-107, 113-118, 201-203, 211-215, 221 and 222 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hoon et al.

The Office Action indicates that the reference teaches a sequence which encodes a polypeptide with over 70% sequence identify with the subject hT1R2 polypeptide which allegedly would be anticipated to hybridize under conditions that "could be considered stringent hybridization conditions".

It is anticipated that this rejection has been rendered moot as the present claims now require that the sequence hybridize under defined stringent hybridization conditions and further require that the claimed nucleic acid sequences encode an hT1R2 polypeptide that is a functional sweet receptor with expressed in association with hT1R3 polypeptide.

Thus no evidence that the Hoon nucleic acid sequence will hybridize under the recited hybridization conditions. Nor is there any evidence or reason to believe it encodes a polypeptide that functions as a sweet receptor when expressed in association with the hT1R3 polypeptide contained in SEQ ID NO: 4.

Withdrawal of the § 102(b) rejection based on Hoon et al is respectfully requested.

Claims 7-11, 17-21, 27-31, 37-41, 59-63, 70-75, 83-87, 95-99, 103-115, 204-208, and 216-220 also stand rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Krautwurst.

Krautwurst discloses a GPCR (olfactory receptor) rhodopsin fusion protein and corresponding nucleic acid sequence. The reference is otherwise irrelevant to the claims.

It is anticipated based on the present amendments that this rejection will not be maintained against any of the current claims. Applicants respectfully submit that none of the newly submitted claims read on the chimeric or fusion nucleic acid sequence disclosed by Krautwurst et al.

Claims 7-11, 27-31, 47-41, 71-75, 83-87, 95-99, 104-112 and 216-220 further stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hoon et al (*Id*) in view of Krautwurst et al (*Id.*).

For similar reasons to these set forth above, it is anticipated that this rejection is also moot in view of the present amendments. Essentially, Hoon et al does not teach or suggest a nucleic acid sequence that meets the limitations of the claims since there is no evidence or reason to conclude that the disclosed nucleic acid sequence will hybridize to the sequence contained in SEQ ID NO: 20 according to the recited defined stringent hybridization conditions recited in claims 235 or that it encodes a hT1R2 polypeptide which when expressed in association with the hT1R3 polypeptide contained in SEQ ID NO: 4 produces a heteromeric functional sweet receptor.

Krautwurst further does not cover the deficiencies of the § 103 rejection since the reference similarly fails to teach or suggest a hT1R2 nucleic acid sequence according to the claims. Rather, the reference is only cited based on a GPCR (olfactory receptor)-rhodopsin DNA fusion.

Based on the foregoing, withdrawal of the § 103 rejection based on Hoon et al. in view of Krautwurst is respectfully requested.

The Examiner's indication of allowable subject matter is also acknowledged with appreciation. It is anticipated that the present amendments and remarks should place all of the claims of this application in condition for allowance. A Notice to that effect is respectfully solicited.

If any issues remain outstanding, the Examiner is respectfully requested to contact the undersigned so that prosecution may be expedited.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #100337.54289US).

Respectfully submitted,

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